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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,386	05/15/2006	Jonathon Mark Tinsley	GRT/117-585	6582

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EXAMINER
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STOICA, ELLY GERALD

ART UNIT	PAPER NUMBER
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1647

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/579,386	<b>Applicant(s)</b> TINSLEY, JONATHON MARK	
	<b>Examiner</b> ELLY-GERALD STOICA	<b>Art Unit</b> 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 November 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-17 and 43-59 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-17 and 43-59 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election without traverse of inventions of group I (claims 1-17 and 43-59) and of the following species: (A) an antibody or antigen-binding fragment thereof, (B) label displacement, (C) a radioisotope, (D) measurement of reporter gene expression, and (E) a membrane fraction from cells expressing the CCRL2 polypeptide are elected, in the reply filed on 11/30/2007 is acknowledged. Examiner is removing the requirement of election of species for category A.

### ***Status of the claims***

2. In the amendment filed 11/30/2007 Applicant cancelled claims 18- 42 and amended claims 2, 3, 17 and 46 and added claims 47-59. Claims 1-17 and 43-59 are pending and are being examined.

### ***Claim Objections***

3. Claim 46 is objected to because of the following informalities: in line 4 of the claim, after "which" the word "is" is missing. Appropriate correction is required.

Claims 4, 6, 8, 10, 17 and 43 are objected to because of the following informalities: they contain non-elected subject matter, there being no allowable generic claim. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-17 and 43,-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Specifically the claims are drawn to a method of detecting an agent that modulates the activity of CCRL2, the method comprising: (a) contacting a CCRL2 polypeptide with a macrophage inflammatory protein-4 (MIP-4) polypeptide in the presence of a candidate agent under conditions, which in the absence of the test agent, permit the binding of the MIP-4 polypeptide to the CCRL2 polypeptide; and (b) determining whether the candidate agent is capable of modulating the interaction between said CCRL2 polypeptide and said MIP-4 polypeptide. The MIP-4 polypeptide is a polypeptide comprising: (a) the sequence shown in SEQ ID NO: 6; or (b) a sequence which is at least 50%-95% identical to the sequence shown in SEQ ID NO: 6 and which binds to and activates a signaling activity of CCRL2; or a fragment of SEQ ID NO: 6 which binds to and activates a signaling activity of CCRL2. The CCRL2 polypeptide is a polypeptide comprising: (a) the sequence shown in SEQ ID NO: 2 or 4; or (b) a sequence which is at least 80% -95% identical to SEQ ID NO: 2 or 4 over its entire length and functionally equivalent to CCRL2; or (c) a fragment of SEQ ID NO: 2 or 4 which is functionally equivalent to CCRL2.

The claims do not require that the polypeptides possess any particular conserved structure which is responsible for the functional property of mutual binding. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Moreover, the specification does not disclose any portion of the polypeptides (be it MIP-4 or CCRL-2) that is responsible of the binding between the two molecules. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Additionally, the description of one polypeptide species for the MIP-4 genus (SEQ. ID. NO.: 6) and two polypeptide species for the CCRL2 genus (SEQ. ID. NOS.: 2 or 4) is not adequate written description of an entire genus of functionally equivalent polypeptides which incorporate all variants and fragments and with at least 50%, 80%, 90%, and 95% sequence identity to polypeptides comprising either sequence of SEQ. ID. NO.: 6 or SEQ. ID. NOS.: 2 or 4, respectively.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*” (See page 1117). The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed” (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above (Seq. Id. Nos.: 2, 4 and 6) the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the methods using the polypeptide sequences consisting of the sequence of Seq. Id. Nos.: 2, 4 and 6, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded

that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

6. Claims 1-17 and 43-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of detection comprising polypeptides of Seq. Id. Nos.: 4 and 6, does not reasonably provide enablement for the method comprising the usage of functionally equivalent polypeptides which incorporate Seq. Id. No.: 2 or for all variants and fragments and with at least 50%, 80%, 90%, and 95% sequence identity to polypeptides comprising either sequence of SEQ. ID. NO.: 6 or SEQ. ID. NOS.: 4, respectively. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is “undue” include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

As presented supra, the claims are drawn to a method of detecting an agent that modulates the activity of CCRL2, the method comprising: (a) contacting a CCRL2 polypeptide with a macrophage inflammatory protein-4 (MIP-4) polypeptide in the

presence of a candidate agent under conditions, which in the absence of the test agent, permit the binding of the MIP-4 polypeptide to the CCRL2 polypeptide; and (b) determining whether the candidate agent is capable of modulating the interaction between said CCRL2 polypeptide and said MIP-4 polypeptide. The novelty of the method lies not in the polypeptides mentioned but in the fact that they were not previously known in the art that they interact and that the MIP-4 modulates the activity of the polypeptide CCRL-2 and such a modulation would have been unpredictable. The specification provides working examples for a specific set of conditions, using the polypeptide of Seq. Id. No.: 4 and 6. However, no guidance or direction is disclosed with respect to the specific binding sites of the interacting proteins. There is no guidance or working examples offered for usage of the polypeptide of Seq. Id No. 2. There is no requirement that any specific portion of the interacting proteins to be conserved when employing variants that have between 50-95% identity with the proteins of the Invention. A person of ordinary skill in the art would have to perform undue experimentation to detect the protein variants that could be employed in the methods claimed. Therefore, due to the novelty of the method and the unpredictability of the assay employing variants of the proteins having less than 100% identity with the polypeptides having a Seq. Id. No. 4 or 6, especially in the view of the lack of guidance regarding the structural requirements needed for mutual binding, it is considered that the amount of experimentation needed to perform the method in a manner commensurate with the full scope of the claims is undue

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-17 and 43-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, it is unclear what the relationship between the step a) in the independent claim 1 and step b) is. Moreover the significance of the recitation “modulating the interaction” is not clear. Is it modulation of binding step, of the signaling pathway or of the effects of the interaction between CCRL2 and MIP-4? Also, in claim 1, the “test agent” recited in the line 5 lacks antecedent basis. Finally, “determining” is not, in and of itself, a method step; it is not clear now the determination is to be made. Thus the metes and bounds of the claims could not be determined.

Claim 43 (as the independent kit claim) and the claims 44-53 (as dependent claim) are indefinite because they do not specify the relationship between the elements of the kit and if they are contained in a single container or in separate containers. Moreover, the independent claim 43 is indefinite because it contains the recitation “or a polynucleotide encoding a CCRL2 polypeptide”. Since the kit is construed to be related to the method of the invention and the method does not specify any use of a polynucleotide, the claim is indefinite.

Claim 44 also fails to specify the interrelationship between elements. Further, is the “cell transformed” the CCLR2 polypeptide, or an additional agent?

***Closest prior art***

9. The closest prior art is considered Boddeke et al. (WO/2002/057779, 07-2002), Gish et al. (WO/98/01557, 01-1998) and Rosen et al. (WO/96/34891, 11-1996) (all cited by Applicant).

Boddeke et al. teach chemokines and receptors thereof, in particular CRAM-B (which is a synonym of the short form of the CCRL2 of Seq. Id. No. 4 of the instant Application) and their role in neurodegenerative or neuroinflammatory disease. Also taught are methods for identifying a candidate drug compound for the treatment of said disease comprising testing said compound for its capacity to modulate or mimic MCP-1 binding with CRAM-B. Putative modulators activity is tested on chemotaxis and calcium signaling (p. 2, line 20 to p. 4, line 5; p. 6, line 13 to p. 7, line 27; p. 10, line 15 to p. 11 line 11; p. 14, line 6 to p. 15 line 14; claims 1-7 and 14).

Gish et al. (WO/98/01557, 01-1998) discloses chemokines, in particular CRAM-A (which is a synonym of the CCRL2 - long version- having the Seq. Id. No. 2 of the instant Application) identified as SEQ ID. NO: 12 by Gish et al. The document teaches reagents related to CRAM-A, including specific antibodies and chemokine receptors. Methods of using said agents for diagnosis and treatment of diseases including inflammatory conditions and diagnostic kits are also mentioned (p. 5, lines 11-29; p. 24, line 20 to p. 26, line 30; p. 45, line 7 to p. 51, line 18).

Rosen et al. (WO/96/34891, 11-1996) discloses the chemokine MIP-4, methods for utilizing MIP-4 for the treatment of a series of disorders including inflammatory disorders, antagonists against MIP-4 and their use as a therapeutic to treat rheumatoid arthritis and inflammatory and infective diseases. Also disclosed are methods for

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screening compounds for identifying agonists or antagonists to the chemokine (p. 9-14; p. 22-33; p. 37-38).

None of the available prior art documents discloses all of the features of independent claim 1 because none discloses that the protein MIP-4 is able to bind to CCRL2. Neither Boddeke et al. nor Gish et al. suggests that CCRL2 may be a receptor for MIP-4. Also Rosen et al. do not suggest that MIP-4 may interact with CGRL2. It can therefore be considered that the skilled person would have neither the technical direction, nor the incentive to modify the methods for detecting modulators of CCRL2 activity of Gish et al. in order to arrive at the method of claims 1-17 or the kits of 43-59 which are based on the interaction of MIP-4 with CCRL2.

### ***Conclusion***

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ELLY-GERALD STOICA whose telephone number is (571)272-9941. The examiner can normally be reached on 8:30-17:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lorraine Spector/, Ph.D.

Primary Examiner, Art Unit 1647